REMARKS

Claims 1-4, 7-9 and 37-42 were pending in the instant application. By this amendment, claims 2, 3, 4, 37-39 and 41 have been canceled without prejudice to Applicants' right to pursue the subject matter of the canceled claims in this or other applications. Claims 1, 7, 8, and 42 have been amended, and new Claims 43-49 have been added to clarify the invention. The amendments are fully supported by the specification and claims as originally filed, as indicated hereinbelow.

In particular, Applicants have amended Claims 1, 7, and 8, to recite "comprising the alpha (2) macroglobulin receptor binding domain." Support for the amendment can be found at page 13, line 37; Figure 7B; and page 14, lines 6 and 7. Claims 1, 7 and 8 have been amended to recite "a tumor-specific antigen." Support for this amendment can be found in the specification, at page 8, lines 23-24; page 37, lines 13-15; and page 45, line 29. Claims 1 and 7 have been amended to replace "proliferative disorder" with "cancer or a tumor." Support for the amendment can be found throughout the specification, see page 33, lines 27 and 28; and page 11, line 9. Claim 42 has been amend to delete "proliferative cell disorder." Support for the amendment can be found at page 34, lines 13-15; and page 11, line 9.

Support for new claims 43 and 44 can be found at page 8, line 27 through page 9, line 5; page 16, lines 1 and 2; page 28, lines 4-10; page 15, line 3, and page 53, lines 9-12. Support for new claim 46 can be found at page 52, line 6, through page 53, line 7, lines 22 and 23. Support for new claims 48 and 49 can be found at page 54, lines 25-36.

The amendments are fully supported by the specification and claims as originally filed, and, as such, no new matter has been added. Applicants respectfully request that the amendments and remarks made herein be entered into the record of the instant application.

1. THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH, FOR INDEFINITENESS, SHOULD BE WITHDRAWN

Claims 1-4, 7-9, and 37-42 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The test of definiteness is whether one skilled in the art would understand the bounds of the claim when read in light of the specification. *Orthokinetic Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1 U.S.P.Q.2d 1081 (C.A.F.C. 1986). Thus, according to applicable case law, the requirement of 35 U.S.C. § 112, second paragraph, means that the claims must have a clear and definite meaning when construed in the light of the complete patent document. *Standard Oil Co. v. American Cyanamid Co.*, 774 F.2d 448, 227 U.S.P.Q. 293 (C.A.F.C. 1985).

The Examiner has rejected Claim 1 and dependent claims thereon as indefinite for recitation of the term "amount." The Examiner contends that the metes and bounds of the claims cannot be determined because the actual quantity of the purified molecular complex has not been defined. Applicants respectfully disagree, and submit that the term "amount" in the context of an "amount of a purified molecular complex effective for treatment or prevention of a type of cancer or a tumor" has a clear and definite meaning when read in light of the specification. For a discussion of this issue, the Examiner is directed to MPEP § 2173.05(c) which states:

> The common phrase "an effective amount" may or may not be indefinite. The proper test is whether or not one skilled in the art could determine specific values for the amount based on the disclosure. See *In re Mattison*, 509 F.2d 563, 184 USPQ 484 (CCPA 1975). The phrase "an effective amount . . . for growth stimulation" was held to be definite where the amount was not critical and those skilled in the art would be able to determine from the written disclosure, including the examples, what an effective amount is. *In re Halleck*, 422 F.2d 911,

> 164 USPQ 647 (CCPA 1970). . . . The more recent cases have tended to accept a limitation such as "an effective amount" as being definite when read in light of the supporting disclosure and in the absence of any prior art which would give rise to uncertainty about the scope of the claim. In *Ex parte Skuballa*, 12 USPQ2d 1570 (Bd. Pat. App. & Inter. 1989), the Board held that a pharmaceutical composition claim which recited an "effective amount of a compound of claim 1" without stating the function to be achieved was definite, particularly when read in light of the supporting disclosure which provided guidelines as to the intended utilities and how the uses could be effected.

Thus, according to case law, if the specification provides sufficient guidance as to the intended utilities of compounds and how these uses could be effected, one of skill in the art can readily determine what is an "amount effective" *Ex parte Skuballa*, 12 U.S.P.Q.2d at 1571.

In the instant case, Applicants assert that the "actual quantity of purified complex" need not be defined or even known, as the Examiner contends, because the amount is not critical, and those skilled in the art would be able to determine from the teachings of the specification the amount necessary for treatment or prevention of cancer. The instant specification provides ample guidance as to the intended utilities of purified molecular complexes and how these uses could be effected, one of skill in the art can readily determine an amount effective for treatment or prevention of a type of cancer or a tumor. For example, the specification teaches that based on standard pharmacokenetic parameters, the skilled practitioner would know how to determine precise dosages based on the judgment of the practitioners and each patient's circumstances, *e.g.,* depending upon condition and medical status of the individual patient, according to standard clinical conditions (see, *e.g.,* page 54, lines 7-19). Taking these factors into consideration, the amount necessary to treat or prevent cancer can be readily ascertained by one skilled in the art. Moreover, the specification teaches preferred embodiments that describe specific examples of the quantity of complex to be administered (see page 55, lines 26-31). Therein, the specification teaches administering

an amount of the complex of the invention that is in the range of about 2 to 150 μg, preferably 2 to 50 μg, most preferably about 25 μg, given once weekly for about 4-6 weeks. Thus, one skilled in the art would clearly understand or could easily determine the metes and bounds of the term "effective amount" given the teachings of the specification.

Thus, in view of the description in the specification and applicable case law, the term "effective amount," has a definite meaning to one skilled in the art.

Claims 1 and 7, and dependent claims thereon, have been rejected as indefinite as allegedly unclear as to which diseases are associated with the term "proliferative disorders."

In response, Claims 1, 7, and 8 have been amended to recite "cancer or tumor" rather than "proliferative disorder." Thus, the rejection based on the indefiniteness of the term "proliferative disorder" has been obviated by the amendments to the claims.

Claim 1 and dependent claims thereon are also rejected as indefinite for recitation of the term "antigen." The Examiner contends the term is unclear and is not adequately defined in the specification.

Applicants respectfully assert that the amendment to Claim 1 overcomes the rejection. In particular, Claim 1 has been amended to recite "tumor-specific" antigen and to delete infectious disease antigens, and Claim 43 has been added to encompass this deleted subject matter encompassing antigens of infectious diseases. Tumor-specific antigens are exemplified in Section 5.2.4.1, at page 37, lines 11-24, and also at page 45, line 29, and page 51, lines 4-7 (*e.g.*, carcinoembryonic antigen). With respect to new Claims 43-47, antigens of infectious diseases are adequately described in the specification at page 37, lines 28-36. Thus, given the amendments made herein, together with the description and examples provided in the specification and cited references, one of skill in the art would clearly be able to understand the meaning of the term "antigen" in Claim 1 and new Claims 43-47.

Claims 1, 3, 7, and 37 are rejected as indefinite for recitation of the term "infectious agent." The Examiner contends the term is unclear and is not adequately defined in the specification.

In response, Claims 1 and 7 have been amended to delete "infectious agent," Claims 3 and 37 have been canceled, and new Claims 43 and 44 have been added to encompass the deleted matter and matter of the canceled claims.

In particular, new Claims 43 and 44 have been added to clarify that the infectious agent is derived from an infectious disease. Support for this term can be found repeatedly throughout the specification (*e.g.*, see page 10, lines 22 and 23). The relationship of the infectious agent to the infectious disease is further defined at page 11, lines 5-7, wherein it is taught that the infectious disease is caused by the infectious agent and examples of such agents include viruses, bacteria, fungi, and parasites. Support for a virus as an infectious agent is also found at page 33, line 36. One skilled in the art would clearly understand the meaning of "infectious agent" of an infectious disease, given the examples and meaning of the term taught in the specification. As such, Applicants submit that this rejection has been obviated and/or overcome with respect to claims 1, 3, 7, 37, 43, and 44.

Claims 8 and 9 are rejected as indefinite for recitation of the term "at least 65%." The Examiner contends it is unclear as to how this is to be measured and what other compounds or molecules will be representing the other 35% of the purified complexes.

Applicants respectfully disagree. The phrase "at least 65%" has a clear and definite meaning, *i.e.*, a purified population of molecular complexes having 65% or greater of the complexes having alpha (2) macroglobulin molecules non-covalently associated with an antigenic molecule (see page 36, lines 23-27). As for the remaining complexes, one of skill in the art would clearly recognize that the remaining 35% of less must be complexes other than non-covalent complexes, *e.g.*, alpha (2) macroglobulin molecules covalently associated

with an antigenic molecule.

Moreover, the skilled artisan would have no difficulty preparing such covalent and noncovalent complexes in appropriate amounts to make a purified population of molecular complexes *in vitro,* wherein at least 65% comprises noncovalent complexes of alpha (2) macroglobulin molecules and antigenic molecules. Given the teachings of the instant specification and the knowledge available in the art, the skilled artisan would know how to measure the amount of non-covalent complexes within a mixture of covalent and non-covalent complexes. For example, the skilled artisan could measure the fraction of noncovalent complexes of alpha (2) macroglobulin molecules within a mixture of covalent and non-covalent complexes by labeling a component of such complexes (*e.g.*, an antigenic peptide), removing the non-covalent complexes from the mixture, and measuring the amount of labeled component (*e.g.*, labeled antigenic peptide) remaining using standard assays (eg, see methods for labeling and detection of proteins on page 26, line 10 through page 28, line 12; page 38, lines 12-22; page 58, lines 34-37; page 33, lines 11-17; page 35, line 9 through page 36, line 30; and page 36, lines 4-15).

In view of the forgoing reasoning and amendments, Applicants respectfully request the Examiner's withdrawal of the rejections under 35 U.S.C. § 112, second paragraph.

2. THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, FOR LACK OF ENABLEMENT SHOULD BE WITHDRAWN

Claims 1-4, 7-9, and 37-42 have been rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an alpha (2) macroglobulin (α 2M) acting as an antagonist to HSP-antigen complexes, allegedly does not reasonably provide enablement for a composition or purified α 2M-peptide complex that has a non-covalently associated antigen with antigenicity of an infectious agent or of a tumor-specific

antigen used for the treatment or prevention of an infectious disease or a proliferative disorder.

The test for enablement is whether one reasonably skilled in the art could make or use the invention, without undue experimentation, from the disclosure in the patent specification coupled with information known in the art at the time the patent application was filed. *U.S. v. Telectronics Inc.*, 857 F.2d 778, 8 U.S.P.Q.2d 1217 (Fed. Cir. 1988). In fact, well known subject matter is preferably omitted. See *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986) ("a patent need not teach, and preferably omits, what is well know in the art."). Further, one skilled in the art is presumed to use the information available to him in attempting to make or use the claimed invention. See *Northern Telecom, Inc. v. Datapoint Corp.*, 908 F.2d 931, 941 (Fed. Cir. 1990) ("A decision on the issue of enablement requires determination of whether a person skilled in the pertinent art, using the knowledge available to such a person and the disclosure in the patent document, could make and use the invention without undue experimentation."). These enablement rules preclude the need for the patent applicant to "set forth every minute detail regarding the invention." *Phillips Petroleum Co. v. United States Steel Corp.*, 673 F. Supp. 1278, 1291 (D. Del. 1991); see also *DeGeorge v. Bernier*, 768 F.2d 1318, 1323 (Fed. Cir. 1985).

Undue experimentation is experimentation that would require a level of ingenuity beyond what is expected from one of ordinary skill in the field. *Fields v. Conover*, 170 U.S.P.Q. 276, 279 (C.C.P.A. 1971). The factors that can be considered in determining whether an amount of experimentation is undue have been listed in *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Among these factors are: the amount of effort involved, the guidance provided by the specification, the presence of working examples, the amount of pertinent literature and the level of skill in the art. The test for undue

experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, so long as it is merely routine. *Id.*

Further, while the predictability of the art can be considered in determining whether an amount of experimentation is undue, mere unpredictability of the result of an experiment is not a consideration. Indeed, the Court of Custom and Patent Appeals has specifically cautioned that the unpredictability of the result of an experiment is not a basis to conclude that the amount of experimentation is undue in *In re Angstadt*, 190 U.S.P.Q. 214 (C.C.P.A. 1976):

> [If, to fulfill the requirements of 112, first paragraph, an applicant's] disclosure must provide guidance which will enable one skilled in the art to determine, with reasonable certainty before performing the reaction whether the claimed product will be obtained, ... then all "experimentation" is "undue" since the term "experimentation" implies that the success of the particular activity is uncertain. Such a proposition is contrary to the basic policy of the Patent Act.
>
> *Id.* at 219 (emphasis in the original).

Finally, case law has resolved that not all embodiments of an invention need be effective. The presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled. The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art. *Atlas Powder Co. v E. I. Du Pont* 750 F2d. 1569.

In light of the legal standard discussed *supra*, Applicants submit that the instant application provides sufficient teaching to enable one of skill in the art to make and use the compositions of the invention that encompass complexes of α2M noncovalently associated with antigenic molecules, without undue experimentation.

The Examiner's rejection is based on the contention that the application does not teach the actual construction of any specific composition or the isolation of a molecular

complex comprising α2M associated with an antigen derived from an infectious disease or cancer. As a result, the Examiner contends that the specification does not teach the actual use of any specific composition or the isolation of a molecular complex comprising α2M associated with an antigen derived from an infectious disease or from a cancer, and that only use of gp96 or α2M to antagonize each other in binding to the α2M receptor is enabled.

The Examiner contends that one skilled in the art would be forced to do undue experimentation to determine a multitude of factors, such as: 1) the possibility that the claimed complexes might elicit an autoimmune response; 2) binding of the α2M polypeptide to the receptor; 3) the ability of the α2M peptide to elicit an MCH I immune response; 4) proliferative diseases encompassed by the invention; 5) the determination of the antigen to be used; and 6) the prevention of disease such as cancer and HIV.

Applicants disagree, and submit that the Examiner has focused on the working example presented in the specification, which discloses the use of gp96 or α2M to antagonize each other, and not the teachings of the specification as a whole. First, the Examiner contends that the skilled artisan would be forced to determine if the desired composition would elicit and autoimmune response. Applicants submit that this amount of routine testing would not be considered undue experimentation. The specification clearly teaches numerous tests which one of skill in the art can use to determine if an immune response has been elicited, including an autoimmune response. For example, Section 5.3.5.1, at page 49, teaches delayed hypersensitivity skin test designed to indirectly test if an antigen elicits an immune response, Section 5.3.5.2, at page 50, teaches *in vitro* activation of cytotoxic T cells, and Section 5.3.5.3. The T-cell assays in particular can be carried out with and without stimulator tumor cells as described in the specification. One skilled in the art could readily compare cells of the same type *in vitro*, where one sample is cancerous and one is normal, to determine if an immune response is specific to a tumor cell or all cells of a

particular type. Thus, one skilled in the art can follow the teachings of the specification and select for compositions that elicit an immune response, that is not an autoimmune response, without resorting to undue experimentation. NO

Second, the Examiner has pointed out that recognition of the α2M receptor by the α2M complex of the invention is necessary for one to use the composition of the invention. In response, Applicants have amended claims 1 and 7 to recite "comprising the alpha (2) macroglobulin receptor binding domain." This language has also been incorporated into new Claims 43, 44, and 47. Thus, the claims as amended now clearly reflect the invention as described in the specification. As such, the rejection based on ability of the complex to bind the receptor has been overcome and should be withdrawn. OK

Third, the Examiner contends that one skilled in the art must determine whether the antigen elicits an MHC class I or II response, before complexing with the α 2M peptide. Applicants respectfully disagree, and assert that one skilled in the art need not know the exact mechanisms or pathways by which the complexes function to follow the teachings of the specification and successfully make and use the claimed compositions. If one skilled in the art can successfully employ the methods taught in the specification for eliciting immune responses as described above, then the claimed invention is enabled. OK

Fourth, the Examiner contends the skilled artisan would be required to determine which proliferative diseases are encompassed by the claimed methods and would need to experiment to determine if antigens associated with other types of proliferative diseases can be used in the claimed compositions.

The specification teaches how to select antigens for use in compositions of the invention that are specific to cancers. In response, Applicants have amended claims 1, 7, and 8 to replace "proliferative disorders" with "cancer or tumor." Applicants assert that experimentation to determine if antigens are tumor-specific would not be undue. Such OK

tumor-specific antigens are well known in the art and can be readily determined using the teachings of the specification. For example, at page 38, lines 13-28, of the specification, methods for determining the immunogenicity or antigenicity of a putative antigen are taught and references for such methods are cited. Following the teaching of the specification, one skilled in the art could select an antigen for any type of cancer, and test a complex comprising the antigen for use in the claimed composition of the invention without resorting to undue experimentation.

Fifth, the Examiner contends the claims encompass "any and all" antigens, and therefore one skilled in the art would need to engage in undo experimentation to determine which antigens are capable of eliciting an immune response. Applicants respectfully submit that amended Claims 1 and 7 recite "tumor-specific antigens," and new Claims 43 and 44 recite "displays the antigenicity of an antigen of an infectious agent," and thus do not encompass any and all antigens. As described above, the specification provides sufficient teaching to enable one skilled in the art to select antigens with particular antigenicity and produce antigenic molecules that elicit an immune response.

Moreover, the results presented in Noguchi *et al.* (page 3172, second column of Noguchi *et al.*, 1994, PNAS 91:3171-3175; "EL" on the Supplemental Information Disclosure Statement ("IDS") submitted concurrently herewith) demonstrate that mixtures of Meth A peptides, such as the large array used in Binder *et al.* (Binder *et al.*, 2001, Journal of Immunology 166:4968-4972, hereinafter "Binder I"; "EJ" on IDS), described below for generating complexes with alpha (2) macroglobulin, contain tumor-specific antigens. Thus, one skilled in the art would not need to resort to identifying tumor-specific antigens to make a composition comprising complexes of alpha (2) macroglobulin and tumor-specific antigens. Assuming one skilled in the art desired to identify tumor-specific antigens, the specification teaches methods for accomplishing identification. For example, at page 38, lines 13-28, of

the specification, methods for determining the immunogenicity or antigenicity of a putative antigen are taught and references for such methods are disclosed. Using these methods, the skilled artisan could select an antigen for any type of cancer and test a complex comprising the antigen for use in the claimed composition of the invention without resorting to undue experimentation. Thus, following the teachings of the specification, one skilled in the art could make compositions comprising complexes of alpha (2) macroglobulin with tumor-specific antigens and use the compositions to treat cancer or tumors without engaging in undue experimentation.

Sixth, the Examiner contends that one skilled in the art would need to engage in undue experimentation to determine if the compositions of the invention can prevent diseases, including cancer and HIV. Applicants respectfully disagree. The specification teaches examination of the antigen's involvement in neutralization of a pathogen's infectivity, which directly relates to prevention of infection (see page 38, lines 29-37). With respect to diseases which have no known preventative vaccines, Applicants point out, in accordance with case law, that not all embodiments of an invention need be operative. It is entirely plausible that one skilled in the art could follow the teachings of the specification and make and successfully use a composition effective for treating HIV or cancer.

As further evidence that one skilled in the art would not need to engage in undo experimentation to make and use the compositions of the invention, Applicants submit herewith articles published subsequent to the filing date of the application, Binder I, discussed above, and Binder *et al.*, 2002, Cancer Immunity 2:16 ("EI" on IDS), hereinafter "Binder II." The experimental results presented in the articles demonstrate that one skilled in the art, following the teachings of the specification (see Sections 5.3.1 and 5.3.2 beginning at page 41), can make complexes of alpha (2) macroglobulin and antigenic molecules for treatment of disease.

Binder II describes non-covalent alpha (2) macroglobulin-OVA peptide complexes which were generated using synthetic OVA20 peptide containing the CTL epitope of OVA. Mice were administered the complex, then challenged with tumor cells expressing OVA, a specific antigen is not expressed in any other cells in the mice. The results presented in Figure 2b, at page 3, demonstrate that alpha (2) macroglobulin complexed to the OVA20 antigen elicited tumor rejection in mice challenged with tumors expressing OVA. The results demonstrate in a mouse model of tumor immunity that alpha (2) macroglobulin complexed to a tumor-specific antigen can successfully be used in compositions for treatment of cancers or tumors using the teachings of the instant application without engaging in undue experimentation.

Figure 2c of Binder II demonstrates that alpha (2) macroglobulin complexed to a large array of tumor antigens extracted from Meth A tumor cells elicit tumor rejection. Mice were first administered the complexes, then challenged with Meth A. The results demonstrate that, using the teachings of the instant specification, one skilled in the art can successfully identify antigens capable of eliciting an immune response and generate complexes of such antigens and alpha (2) macroglobulin for use in compositions for treatment of cancers and tumors.

Binder I demonstrates the preparation of alpha (2) macroglobulin complexes are capable of priming CTL responses in mice. The results presented in Figure 2, lower panel, for the tumor-specific antigen OVA20 complexed to alpha (2) macroglobulin show that the complexes prime CTL response in mice. Similarly, Figure 2, lower panel, also shows that the viral-derived antigen AH1 complexed to alpha (2) macroglobulin is capable of priming the CTL response in mice (AH-1 is an antigen derived from the MuLV virus, see Huang et al., IDS No. EK). These results evidence the ability of the complexes to elicit an immune response. The results presented in Figure 3 of the Binder I show that the same alpha

(2) macroglobulin-OVA and -AH1 complexes activate T cells in representation assays. The CTL response and T-cell representation results indicate the ability to elicit an immune response and support the use of the complexes in the compositions of the invention for treatment of cancer, tumors, and infectious disease. Thus, the Binder references validate the teachings of the instant specification for making and using alpha (2) macroglobulin complexes for the treatment or prevention of cancer or infectious diseases without undue experimentation.

The above described published *in vivo* results of administration of tumor-specific and viral peptides complexed to alpha (2) macroglobulin also demonstrate the predictability of the compositions of invention. The Examiner contends that the compositions are not enabled in part because, it is unpredictable whether undesirable autoimmune responses would also be induced. Applicants point out that if the overall survival rate increases as demonstrated in the results of Binder I (see Figure 2b) the positive effect of the composition far outweighs any hypothetical undesirable effects. Thus, the results of the Binder references demonstrate the predictability and efficacy of alpha (2) macroglobulin compositions comprising the complexes for the treatment of cancer, tumors, and infectious disease

In light of the foregoing reasoning and amendments, the rejection under 35 U.S.C. § 112, first paragraph for lack of enablement should be withdrawn.

3. THE REJECTION UNDER 35 U.S.C. § 102(b) FOR ANTICIPATION SHOULD BE WITHDRAWN

Claims 1, 3, 4, 7, 8, 38, 39, and 42 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Otto *et al.* (1998, J. Urol 159(1):297-303, "Otto"). The Examiner contends that Otto teaches that prostate specific antigen ("PSA") can associate with the full length α2M protein and that between 95-99% of the complex is in non-covalent

form. Furthermore, the Examiner contends the pharmaceutical composition is anticipated because it is considered to be an intended usage of the basic product, which is a molecular complex comprising a α2M associated with an antigen from a cell which is involved in a proliferate disorder.

In order for a reference to anticipate a claim, each and every element of the claim must be disclosed in that one reference. *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565 (Fed. Cir. 1985). "Anticipation under Section 102 can be found only if a reference shows exactly what is claimed . . ." *Structural Rubber Prod. Co. v. Park Rubber Co.*, 749 F.2d 707 (Fed. Cir. 1984).

As noted above, Applicants have amended claims 1 and 7 to delete "infectious disease" and "infectious antigen," and added new claims 43 and 44 to encompass the deleted matter. The new claims do not encompass proliferative disorder antigens and thus are not anticipated by Otto. Claims 1 and 7 have also been amended to recite "tumor-specific antigens." Applicants assert that PSA is not a tumor-specific antigen, because it is found in both normal and abnormal prostate tissues. See Heiser, 2000, Journal of Immunology, 164(10):5508-5514, page 5513, final paragraph, (reference no. EC on Supplemental IDS submitted concurrently herewith) and Oesterling, 1991, Journal of Urology, 145(5):907-23, page 907, left column, fifth paragraph (reference no. ED on Supplemental IDS submitted concurrently herewith). Therefore, the claims as amended, are not anticipated by Otto.

In view of the amendments and reasoning presented above, Otto does not disclose or suggest the claims of the instant invention. Accordingly, applicants respectfully submit that the rejection under 35 U.S.C.§ 102(b) has been obviated and should be withdrawn.

CONCLUSION

Applicants respectfully request that the present remarks and amendments be entered and made of record in the instant application. Applicants estimate that the remarks and amendments made herein now place the pending claims in condition for allowance. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

It is believed that no fee is required for filing this Reply. In the event a fee is required, please charge the required fee to Pennie & Edmonds LLP Deposit Account No. 16-1150.

Respectfully submitted,

Date: July 30, 2003

Adriane M. Antler — 32,605 (Reg. No.)

By: Eileen E. Falvey — 46,097 (Reg. No.)

PENNIE & EDMONDS LLP
1155 Avenue of the Americas
New York, New York 10036-2711
(212) 790-9090

Enclosures